Autism Spectrum Disorders and Race, Ethnicity, and Nativity: A Population-Based Study

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**ABSTRACT**

Maternal nativity is a risk factor for childhood autism in US populations. We observed higher risk of severe autism phenotypes in children of foreign-born black, Central/South American, Filipino, and Vietnamese mothers and US-born African Americans and Hispanics compared with US-born whites.

**WHAT’S KNOWN ON THIS SUBJECT:** Autism prevalence is reported to be highest among non-Hispanic white children, lower in Hispanic and African American/black children, and highly variable in Asian/Pacific Islanders. More comorbid intellectual disability and delays in expressive language have been observed among Hispanic and African American children.

**WHAT THIS STUDY ADDS:** Maternal nativity is a risk factor for childhood autism in US populations. We observed higher risk of severe autism phenotypes in children of foreign-born black, Central/South American, Filipino, and Vietnamese mothers and US-born African Americans and Hispanics compared with US-born whites.

**METHODS:** Children born in Los Angeles County with a primary AD diagnosis at ages 3 to 5 years during 1998–2009 were identified and linked to 1995–2006 California birth certificates (7540 children with AD from a cohort of 1626354 births). We identified a subgroup of children with AD and a secondary diagnosis of mental retardation and investigated heterogeneity in language and behavior.

**RESULTS:** We found increased risks of being diagnosed with AD overall and specifically with comorbid mental retardation in children of foreign-born mothers who were black, Central/South American, Filipino, and Vietnamese, as well as among US-born Hispanic and African American/black mothers, compared with US-born whites. Children of US African American/black and foreign-born black, foreign-born Central/South American, and US-born Hispanic mothers were at higher risk of exhibiting an AD phenotype with both severe emotional outbursts and impaired expressive language than children of US-born whites.

**CONCLUSIONS:** Maternal race/ethnicity and nativity are associated with offspring’s AD diagnosis and severity. Future studies need to examine factors related to nativity and migration that may play a role in the etiology as well as identification and diagnosis of AD in children.

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For 2 decades, autism prevalence has risen in the United States and now reaches ~147 per 10,000 children diagnosed with autism spectrum disorders (ASDs) by 8 years of age and 21 per 10,000 children with autistic disorder (AD). The associated disabilities are characterized by atypical development of socialization and communication and the presence of restricted, repetitive interests and behaviors beginning in early childhood. Lower ASD prevalence in Hispanic and African American/black children (henceforth “black”) than in non-Hispanic white children (henceforth “white”) and variations in prevalence from 30 to 210 per 10,000 among Asians/Pacific Islanders (Asians/Pis) have been reported. Autism phenotype differences with regard to intellectual and language disabilities across race/ethnic groups in the United States may suggest differences in ASD etiology and disparities in diagnostic and treatment-related factors.

The prenatal period is strongly implicated in ASD etiology; yet, except for parental age and some pregnancy complications, evidence is insufficient for many potential prenatal risk factors, including recently reported associations with immigration status of the mother. Epidemiology has a long tradition of using migration studies to understand how environmental and genetic factors contribute to disease risk in populations. The fact that 22% of children <6 years old born in the United States have immigrant parents opens a unique opportunity to consider the influence of nativity and race/ethnicity on the etiology of ASD.

We hypothesized that the prevalence of AD (Diagnostic and Statistical Manual of Mental Disorders, Revised Fourth Edition [DSM-IV-R]) and specific phenotypes, ie, comorbid mental retardation (MR), expressive language, and emotional/behavioral deficits, differs by maternal race/ethnicity and nativity. We focused our investigation on children born and diagnosed in Los Angeles (LA) County, California, a highly diverse metropolitan region home to black (400,000 in 2010), Hispanic (4.7 million in 2008), and Asian/PI (1.4 million in 2012) residents with a high proportion of immigrants (30% in 2011) and 92 languages spoken by students of the LA Unified School District. Our findings have clinical implications for early identification and treatment of ASD and research implications that raise innovative hypotheses, not only for different racial/ethnic groups but specifically for large and diverse immigrant communities who vary in risk, protective factors, and access to health care.

METHODS

We studied children born to mothers who resided in LA County, California, between 1995 and 2006. Children included in the current study had birth certificate information on maternal race/ethnicity and maternal nativity and a plausible gestational age (21–46 weeks) and birth weight (500–6800 g). Maternal race/ethnicity and nativity were determined on the basis of mother’s self-reported Hispanic origin (yes or no), race (non-Hispanic white, non-Hispanic black, Hispanic, and non-Hispanic Asian), and maternal nativity (US-born or foreign-born). California birth certificates also asked Hispanic mothers to identify their ethnic ancestry and specified country of origin for several Asian and Latin American nations and US territories. Asian ethnic ancestry for US-born mothers was available, but investigating AD in US-born Asian children by country of origin was not possible due to small numbers (138 cases among 21,678 births).

In LA County, children needing assessment and treatment of ASD are seen at a network of 7 regional centers contracted by the California Department of Developmental Services (DDS). Referrals to regional centers are made according to residential address by pediatricians, other clinical providers, and schools; parents can also self-refer their children. During our study period, DDS services were available to all children free of charge irrespective of income, type of health insurance, or immigration status. The diagnosis of AD was based on the DSM-IV-R (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 299.00), as reported on the DDS Client Development Evaluation Report (CDER). The AD diagnoses for these children would likely hold under the new ASD diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).

Validation studies have established the reliability and validity of the CDER. Trained psychologists usually make the diagnostic determination of AD/ASD at 7 DDS regional centers. Best practice suggests that primary care providers provide a comprehensive medical assessment including a health history, physical examination, and developmental/neurologic examination. California published guidelines in 2002 to establish a comprehensive diagnostic evaluation for ASD that encompasses the following: (1) review of relevant background information, (2) parent/caregiver interview, (3) comprehensive medical evaluation, (4) cognitive assessment, (5) measures of adaptive functioning, and (6) direct observation, in which the Autism Diagnostic Observation Scale (ADOS) was recommended tool.

From DDS records, we identified 10,821 children with a primary AD diagnosis at 36 to 71 months of age during 1998–2009 and were able to link 8600 (79.5%) to a California birth record by using a probabilistic linkage program, as described in a previous article.

The main reason for nonlinkage of 2221 DDS records was missing/incomplete information on the birth or DDS records.
In total, 1,626,354 births of which 7540 children had an AD diagnosis were eligible according to our criteria and had a mother of white, black, Hispanic, or Asian/PI race/ethnicity.

We also identified a subgroup of children with AD and a secondary diagnosis of MR (AD-MR), according to DSM-IV terminology from the CDER (ICD-9-CM codes: 317, mild; 318.0, moderate; 318.1, severe; 318.2, profound; 319, MR unspecified). Although we will use the term “mental retardation” in the context of the actual diagnoses, we recognize the changes in terminology to “intellectual disability” in the DSM-5 and will refer to the more accepted “emotional outburst behavior” or “tantrum behavior,” which was previously observed to be an indicator of socioeconmic status (SES). 28 Finally, to consider possible diagnostic variability, we controlled for DDS regional center catchment area (for controls, regional center was according to residential address during birth).

RESULTS

The mean age of children entering the DDS system differed by no more than 6 months by maternal race/ethnicity and nativity (range: 3 years 1 month to 3 years 7 months); children identified earliest were born to US-born Asian, foreign-born Japanese, foreign-born black, and US-born white mothers, whereas those diagnosed later were children of mothers who immigrated from Central/South America and Vietnam.

Crude rates of being diagnosed with AD varied by race/ethnicity and nativity (from 32 to 93 per 10,000 births), and fully adjusted risks were 76% higher in children of foreign-born black mothers, 43% higher in foreign-born Vietnamese, 25% higher in foreign-born Filipinos, 26% higher in foreign-born Central/South Americans, and 13% to 14% higher in US-born Hispanics and blacks compared with US-born white mothers (Table 1). Children whose mothers were born in China and Japan were at ~30% lower risk of AD compared with white US-born children, and adjustment for all available risk factors changed estimates only minimally. Additional adjustment for region of birth center changed the risk of AD only for children of US-born black mothers in a substantive manner and suggested an increased risk.

**AD-MR**

Among 806 children diagnosed with AD-MR (Table 2), the highest crude rates were observed in children of foreign-born black, Vietnamese, and Filipino mothers. Adjustment for other risk factors strengthened estimates with more than twofold increased risks compared with whites. For all children, adjusted risk estimates were >1 (95% confidence intervals included the null values for smaller groups), regardless of maternal nativity, except for Mexican-born mothers.

**AD: Expressive Language Skills and Emotional Outburst Phenotypes**

For 5-year-old children with impaired AD expressive language abilities (Table 3),
most race/ethnicity and nativity subgroups were at higher risk of an impaired expressive language phenotype, which persisted when restricting to children who were diagnosed early (ie, at 2 or 3 years of age; results not shown). Fewer differences for children with a less impaired language phenotype were observed (ie, risks were comparable to US-born whites, except for children of foreign-born Mexican, Chinese, and Korean mothers who were at lower risk).

Considering the 1396 with a “severe” emotional outburst behavior phenotype among 4197 total 5-year-old children with AD, those born to US-born Hispanic and foreign-born Central/South American mothers were at higher risk only in the severe outburst category (Table 4). However, higher risk of severe outbursts only persisted in conjunction with impaired expressive language (results not shown). Children of foreign-born black mothers were at increased risk of both phenotypes, whereas Vietnamese and Filipino offspring exhibited slightly higher risks of AD with the less severe outburst phenotype.

**DISCUSSION**

We investigated the influence of maternal race/ethnicity and nativity on AD diagnosis in LA County, a racially diverse area with a high percentage of recent immigrants. We found compelling evidence that, compared with children born to white US-born mothers, children of foreign-born black, Filipino, and Vietnamese mothers had higher risks of developing or being diagnosed with AD, specifically with MR and impaired expressive language. Previously, immigration status was reported to not be associated with high risk of AD in California,5 possibly due to the lower risks we observed among offspring of foreign-born Mexican women, who make up the majority of the foreign-born population in California (53%).19 However, we found foreign-born black mothers to be at highest risk of having a child with AD and AD-MR and impaired language abilities, consistent with findings of a higher autism risk among children born to refugee mothers from Africa and the Caribbean living in the United Kingdom and Sweden.29–32 Differences in AD risk by race/ethnicity and nativity could imply variation in etiologic factors across racial/ethnic/nativity groups, which might affect fetal or early childhood development, including stress, diet, toxic environmental exposures, or infections.33,34 These differences could also point to disparities in accessing and receiving appropriate diagnosis and treatment.

US minority groups are historically disadvantaged, and it is possible that children with milder symptoms did not go to a regional center and were missed during diagnosis and treatment.

![Downloaded from by guest on April 6, 2017](https://example.com)
Asian/PI  Hispanic  Black  White  cervix, sexually transmitted diseases, hepatitis B, rubella, other infections, prenatal tobacco use, and large gestational age (in US-born Hispanic, black, and white the crude rates were indeed similar.

...treatment, such as the AD-MR and im-

...more likely to prompt identi-

...more severe AD phenotypes that are

...adjustment for these factors

...when we assessed maternal race/

...ethnicity subgroups by nativity and ad-

...adjusted for well-known risk factors such
c...as maternal age, similar or higher AD risks were estimated. SES and location of diagnosis may be related to environ-

...mental risk factors and may also be a source of identification and diagnosis variability. Adjustment for these factors changed a no-risk to a higher-risk esti-

...mung risk factors and may also be a source of identification and diagnosis variability. Adjustment for these factors changed a no-risk to a higher-risk esti-

...US-born Hispanic, black, and white children but higher after adjustment for risk factors. Language and cultural barriers (ie, low access to psychologists from minority groups, appropriately standardized and language-sensitive assessment instruments)35–38 could also have caused underascertainment of AD or misclassification of language skills, a category in which children from all minority groups were at higher risk compared with those with US-born white mothers. Underutilization of formal health services was reported in Chinese and other Asian populations, and underdiagnosis of milder forms of AD at a young age was reported in black children.59,61

...pready physical relocation and is often preceded by uncertainty, with refugees sometimes facing life-threatening sit-

...and underdiagnosis of milder forms of AD at a young age was reported in black children.59,61

...information about AD incidence or preval-

...lum in lower income countries in Africa,52 Latin America, and South East Asia43 is limited, although rates of ASD are reportedly increasing in Vietnam,44 making it difficult to determine whether the observed AD risk reflects rates from country of origin or if it is a migratory phenomenon. Voluntary migration involves physical relocation and is often preceded by uncertainty, with refugees sometimes facing life-threatening situations; after arriving, immigrants may end up in low-SES neighborhoods, becoming socially vulnerable. Women from Central American nations (Guatemala, El Salvador) who migrated seeking asylum in the 1980s may have a history of trauma from civil war, violence, and displacement.45–47 Maternal life event stress and psychiatric disorders, possibly related to experiences of escaping wars and disasters, as well as nutritional deficiencies from famine, may be possible explanations for the increased risks observed in Central American, Vietnamese, and some African immigrant groups.48–53 and are considered risk factors for low-functioning autism in offspring.54,55 Dietary factors such as folic acid and vitamin D deficiencies, common among US black and Hispanic women56,57 and in women from Vietnam and the Philippines,58,59 could explain some of the increased risk of AD and AD-MR.60–65
deficiency in pregnant women is less common in China’s southern regions, from where a majority of US Chinese immigrants originate.64,65 Also, being born and raised in a foreign country may result in less immunity against local host country pathogens, increasing susceptibility to infections common in the United States. Maternal infections can affect fetal brain development, and some authors suggested that influenza and prolonged episodes of fever increase ASD risk.10,66–68 This hypothesis may apply to Filipino mothers, of whom a large proportion (30%) are employed in health care–related occupations in which the risk of exposure to infections is high.69 Studying this common infection hypothesis in more depth, however, is necessary.

Contrary to Central/South American immigrants, children born to immigrant Mexican women were at similar risk to US-born whites for AD and AD-MR. These children were also at lower risk of being diagnosed with "less impaired" language, possibly suggesting under-diagnosis of milder forms of AD. Alternatively, AD differences favoring Mexican immigrants compared with US-born Hispanic Americans, despite similarly lower income and education, resemble the "Latina paradox" of healthier birth outcomes.70–72 Evidence for a Latina paradox is supported by a higher adjusted risk of AD diagnosis among US-born Hispanics, who also had higher risks of more severe phenotypes, including MR, impaired language, and severe emotional outburst behaviors as also seen in an earlier report.73 Although the large and diverse LA population allowed us to assess AD risk in offspring of mothers who migrated from different regions of the world, a comparison with US-born women from the same backgrounds was limited due to smaller subgroup sample size. Because the comparison group was US-born white women, differences in prevalence may also be due to genetic variation according to race/ethnicity. The DDS counts of persons with autism likely underestimate the actual California population because it is estimated that 75% to 80% of the total population of persons with autism in California are enrolled in the developmental service system.74 Although our large sample size did not allow us to validate diagnoses, the diagnostic stability of AD is considered good within the studied age group (the diagnostic consistency for ASD between ages 2 and 9 years is 90%).22,75 Furthermore, our study included children with a diagnosis of AD, which is more likely to hold under DSM-5 criteria (sensitivity: 0.78) than other ASD groups (ie, Asperger syndrome, pervasive developmental disorder, not otherwise specified) (sensitivity: 0.25–0.28).21

### TABLE 3 Maternal Race/Ethnicity and Nativity in Relation to Child’s Diagnosis of AD by Expressive Language Skills at 5 Years of Age

<table>
<thead>
<tr>
<th>Maternal Race/Ethnicity and Nativity</th>
<th>Impaired Expressive Language</th>
<th>Less-Impaired Expressive Language</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case/Cohort, n</td>
<td>Rate, per 10 000 Births</td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US-born</td>
<td>349/197 992</td>
<td>17.6</td>
</tr>
<tr>
<td>Foreign-born</td>
<td>108/51 540</td>
<td>21.1</td>
</tr>
<tr>
<td>Black</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US-born</td>
<td>189/103 645</td>
<td>18.2</td>
</tr>
<tr>
<td>Foreign-born</td>
<td>36/8331</td>
<td>45.6</td>
</tr>
<tr>
<td>Hispanic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US-born</td>
<td>429/250 825</td>
<td>17.1</td>
</tr>
<tr>
<td>Foreign-born</td>
<td>983/595 680</td>
<td>16.7</td>
</tr>
<tr>
<td>Mexico</td>
<td>700/480 141</td>
<td>15.2</td>
</tr>
<tr>
<td>Central/South America</td>
<td>276/139 379</td>
<td>21.1</td>
</tr>
</tbody>
</table>

CI, confidence interval; NA, not applicable; RR, risk ratio.
*Adjusted for maternal age (≤18, 19–25, 26–30, 31–35, or >35 years), type of birth (single or twin+), parity (1, 2, 3, or >3 children), infant gender (male or female), year of birth (1995–2006), gestational age (<37 weeks or ≥37 weeks), birth weight (<2500, 2500–4900, or >4900 g), trimester start of prenatal care (no care, first, second, or third trimester), any pregnancy complication (hypertension, renal, lung, or cardiac disease, asthma, pylonephritis, diabetes, gestational diabetes, Rh sensitivity, hemoglobinopathy, uterine bleeding, hydramnios, incomplete cervices, sexually transmitted diseases, hepatitis B, rubella, other infections, prenatal tobacco use, and large fibroids), maternal education (less than high school, high school, more than high school), insurance type (Medi-Cal, private insurance, other), and regional center. Language information is presented for cases 5 years of age at evaluation; cohort is for 1995–2004 births, N = 1 340 850.
CONCLUSIONS

Our results underscore the importance of ASD research in diverse racial/ethnic populations that considers nativity to inform clinical practice. Systematic exploration of risk and protective factors related to living circumstances before and after migration is sorely needed and may lead to clinical and public health interventions (ie, mental health, environmental, or dietary interventions).

Exploring infections and immunologic profiles across immigrant subgroups, their exposures to stress and environmental factors, as well as the role of acculturation and adoption of the new culture’s diet may be particularly important and informative. Equally important is the need to improve quality of and access to health care for diverse populations to improve autism diagnoses and timeliness of treatment.

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